

Israeli R.S., Powell C.T., Fair W.R., Heston W.D.W.;

RT "Molecular cloning of a complementary DNA encoding a prostate-specific  
 RT membrane antigen.";

RL Cancer Res. 53:227-230(1993).

RN [2]

RP NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM PSMA').

RC TISSUE=Prostate;

RX MEDLINE=95188188; PubMed=7882349;

RA Su S.L., Huang I.-P., Fair W.R., Powell C.T., Heston W.D.W.;

RT "Alternatively spliced variants of prostate-specific membrane antigen  
 RT RNA: ratio of expression as a potential measurement of progression.";

RL Cancer Res. 55:1441-1443(1995).

RN [3]

RP NUCLEOTIDE SEQUENCE [MRNA] (ISOFORMS PSMA-1 AND PSMA-2).

RC TISSUE=Prostate;

RX MEDLINE=98041505; PubMed=9375657;

RA Bzdega T., Turi T., Wroblewska B., She D., Chung H.S., Kim H.,  
 RA Neale J.H.;

RT "Molecular cloning of a peptidase against N-acetylaspartylglutamate  
 RT from a rat hippocampal cDNA library.";

RL J. Neurochem. 69:2270-2277(1997).

RN [4]

RP NUCLEOTIDE SEQUENCE [GENOMIC DNA] (ISOFORM PSMA-1), AND VARIANT  
 RP HIS-75.

RX MEDLINE=99057588; PubMed=9838072; DOI=10.1016/S0167-4781(98)00200-0;

RA O'Keefe D.S., Su S.L., Bacich D.J., Horiguchi Y., Luo Y., Powell C.T.,  
 RA Zandvliet D., Russell P.J., Molloy P.L., Nowak N.J., Shows T.B.,  
 RA Mullins C., Vonder Haar R.A., Fair W.R., Heston W.D.W.;

RT "Mapping, genomic organization and promoter analysis of the human  
 RT prostate-specific membrane antigen gene.";

RL Biochim. Biophys. Acta 1443:113-127(1998).

RN [5]

RP NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM PSMA-1).

RC TISSUE=Brain;

RX MEDLINE=98362085; PubMed=9694964;

RA Luthi-Carter R., Barczak A.K., Speno H., Coyle J.T.;

RT "Molecular characterization of human brain N-acetylated alpha-linked  
 RT acidic dipeptidase (NAALADase).";

RL J. Pharmacol. Exp. Ther. 286:1020-1025(1998).

RN [6]

RP NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM PSMA-1), AND CHARACTERIZATION.

RC TISSUE=Prostate;

RX MEDLINE=99185063; PubMed=10085079; DOI=10.1074/jbc.274.13.8470;

RA Pangalos M.N., Neefs J.-M., Somers M., Verhasselt P., Bekkers M.,  
 RA van der Helm L., Fraiponts E., Ashton D., Gordon R.D.;

RT "Isolation and expression of novel human glutamate carboxypeptidases  
 RT with N-acetylated alpha-linked acidic dipeptidase and dipeptidyl  
 RT peptidase IV activity.";

RL J. Biol. Chem. 274:8470-8483(1999).

RN [7]

RP NUCLEOTIDE SEQUENCE [MRNA] (ISOFORMS PSMA-1 AND PSMA-2), AND VARIANT  
 RP TYR-475.

RC TISSUE=Jejunum;

RX PubMed=11092759; DOI=10.1093/hmg/9.19.2837;

RA Devlin A.M., Ling E.-H., Peerson J.M., Fernando S., Clarke R.,  
 RA Smith A.D., Halsted C.H.;

RT "Glutamate carboxypeptidase II: a polymorphism associated with lower  
 RT levels of serum folate and hyperhomocysteinemia.";

RL Hum. Mol. Genet. 9:2837-2844(2000).

RN [8]

RP NUCLEOTIDE SEQUENCE [GENOMIC DNA] (ISOFORM PSMA-5).

RA Peace D.J., Zhang Y., Holt G., Ferrer K.T., Heller M., Sosman J.A.,  
 RA Xue B.H.;

RT "Identification of three novel splice variants of prostate-specific  
 RT membrane antigen.";

RL Submitted (NOV-1998) to the EMBL/GenBank/DDBJ databases.

RN [9]

RP NUCLEOTIDE SEQUENCE [MRNA], AND TISSUE SPECIFICITY.

RC TISSUE=Liver;

RX PubMed=14716746; DOI=10.1002/pros.10319;

RA O'Keefe D.S., Bacich D.J., Heston W.D.W.;

RT "Comparative analysis of prostate-specific membrane antigen (PSMA)  
 RT versus a prostate-specific membrane antigen-like gene.";  
 RL Prostate 58:200-210(2004).  
 RN [10]  
 RP PARTIAL NUCLEOTIDE SEQUENCE [MRNA] (ISOFORMS PSMA-3 AND PSMA-4).  
 RA Lupold S.E., Criley S.C., Coffey D.S.;  
 RT "Alternative Splicing of the prostate-specific membrane antigen.";  
 RL Submitted (APR-2000) to the EMBL/GenBank/DBJ databases.  
 RN [11]  
 RP PROTEIN SEQUENCE OF 60-74, AND SUBCELLULAR LOCATION.  
 RC TISSUE=Prostatic carcinoma;  
 RX MEDLINE=99025849; PubMed=9809977;  
 RA Grauer L.S., Lawler K.D., Maignac J.L., Kumar A., Goel A.S.,  
 RA Wolfert R.L.;  
 RT "Identification, purification, and subcellular localization of  
 RT prostate-specific membrane antigen PSM' protein in the LNCaP prostatic  
 RT carcinoma cell line.";  
 RL Cancer Res. 58:4787-4789(1998).  
 RN [12]  
 RP ALTERNATIVE SPLICING.  
 RA Bzdega T., She D., Turi T., Wroblewska B., Neale J.H.;  
 RT "Molecular cloning of alternatively spliced variants of the peptidase  
 RT against N-acetylaspartylglutamate (NAAG) from human and rat nervous  
 RT systems.";  
 RL Abstr. - Soc. Neurosci. 24:579-579(1998).  
 RN [13]  
 RP CHARACTERIZATION.  
 RX MEDLINE=98288196; PubMed=9622670; DOI=10.1016/S0006-8993(98)00244-3;  
 RA Luthi-Carter R., Barczak A.K., Speno H.D., Coyle J.T.;  
 RT "Hydrolysis of the neuropeptide N-acetylaspartylglutamate (NAAG) by  
 RT cloned human glutamate carboxypeptidase II.";  
 RL Brain Res. 795:341-348(1998).  
 RN [14]  
 RP DOMAIN STRUCTURE.  
 RX MEDLINE=97330810; PubMed=9187245; DOI=10.1016/S0167-4838(97)00008-3;  
 RA Rawlings N.D., Barrett A.J.;  
 RT "Structure of membrane glutamate carboxypeptidase.";  
 RL Biochim. Biophys. Acta 1339:247-252(1997).  
 RN [15]  
 RP MUTAGENESIS.  
 RX MEDLINE=99102317; PubMed=9882712;  
 RA Speno H.S., Luthi-Carter R., Macias W.L., Valentine S.L.,  
 RA Joshi A.R.T., Coyle J.T.;  
 RT "Site-directed mutagenesis of predicted active site residues in  
 RT glutamate carboxypeptidase II.";  
 RL Mol. Pharmacol. 55:179-185(1999).  
 RN [16]  
 RP GLYCOSYLATION AT ASN-76; ASN-336; ASN-459; ASN-476 AND ASN-638.  
 RX MEDLINE=22660472; PubMed=12754519; DOI=10.1038/nbt827;  
 RA Zhang H., Li X.-J., Martin D.B., Aebersold R.;  
 RT "Identification and quantification of N-linked glycoproteins using  
 RT hydrazide chemistry, stable isotope labeling and mass spectrometry.";  
 RL Nat. Biotechnol. 21:660-666(2003).  
 RN [17]  
 RP GLYCOSYLATION AT ASN-51; ASN-76; ASN-121; ASN-140; ASN-153; ASN-195;  
 RP ASN-336; ASN-459; ASN-476 AND ASN-638, AND MUTAGENESIS OF ASN-51;  
 RP ASN-76; ASN-121; ASN-140; ASN-153; ASN-195; ASN-336; ASN-459; ASN-476;  
 RP ASN-638 AND THR-640.  
 RX PubMed=15152093; DOI=10.1110/ps.04622104;  
 RA Barinka C., Sacha P., Sklenar J., Man P., Bezouska K., Slusher B.S.,  
 RA Konvalinka J.;  
 RT "Identification of the N-glycosylation sites on glutamate  
 RT carboxypeptidase II necessary for proteolytic activity.";  
 RL Protein Sci. 13:1627-1635(2004).  
 CC -!- FUNCTION: Has both folate hydrolase and N-acetylated-alpha-linked-  
 CC acidic dipeptidase (NAALADase) activity. Has a preference for tri-  
 CC alpha-glutamate peptides. In the intestine, required for the  
 CC uptake of folate. In the brain, modulates excitatory  
 CC neurotransmission through the hydrolysis of the neuropeptide, N-  
 CC acetylaspartylglutamate (NAAG), thereby releasing glutamate.  
 CC Isoforms PSM-4 and PSM-5 would appear to be physiologically

CC irrelevant. Involved in prostate tumor progression.  
 CC -!- FUNCTION: Also exhibits a dipeptidyl-peptidase IV type activity.  
 CC In vitro, cleaves Gly-Pro-AMC.  
 CC -!- CATALYTIC ACTIVITY: Release of an unsubstituted, C-terminal  
 CC glutamyl residue, typically from Ac-Asp-Glu or folylpoly-gamma-  
 CC glutamates.  
 CC -!- COFACTOR: Binds 2 zinc ions per subunit. Required for NAALADase  
 CC activity.  
 CC -!- ENZYME REGULATION: The NAALADase activity is inhibited by beta-  
 CC NAAG, quisqualic acid, 2-(phosphonomethyl) pentanedioic acid  
 CC (PMPA) and EDTA. Activated by cobalt.  
 CC -!- BIOPHYSICOCHEMICAL PROPERTIES:  
 CC pH dependence:  
 CC Stable at pH greater than 6.5;  
 CC -!- SUBCELLULAR LOCATION: Cell membrane; Single-pass type II membrane  
 CC protein. Isoform PSMA': Cytoplasm.  
 CC -!- ALTERNATIVE PRODUCTS:  
 CC Event=Alternative splicing; Named isoforms=6;  
 CC Comment=Experimental confirmation may be lacking for some  
 CC isoforms;  
 CC Name=PSMA-1;  
 CC IsoId=Q04609-1; Sequence=Displayed;  
 CC Name=PSMA-2;  
 CC IsoId=Q04609-2; Sequence=VSP\_005341;  
 CC Name=PSMA-3;  
 CC IsoId=Q04609-3; Sequence=VSP\_005342;  
 CC Name=PSMA-4;  
 CC IsoId=Q04609-4; Sequence=VSP\_005339, VSP\_005340;  
 CC Name=PSMA-5;  
 CC IsoId=Q04609-5; Sequence=VSP\_005337, VSP\_005338;  
 CC Name=PSMA';  
 CC IsoId=Q04609-6; Sequence=VSP\_005336;  
 CC -!- TISSUE SPECIFICITY: Highly expressed in prostate epithelium. Also  
 CC expressed, in the small intestine, brain, kidney, liver, spleen,  
 CC colon, trachea, spinal cord and the capillary endothelium of a  
 CC variety of tumors. Expressed specifically in jejunum brush border

Query Match 100.0%; Score 3983; DB 1; Length 750;  
 Best Local Similarity 100.0%; Pred. No. 1.6e-266;  
 Matches 750; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MWNLLHETDSAVATARRPRWLCAGALVLAGGFLLGFLFGWFIKSSNEATNITPKHNMKA 60
Db      1 MWNLLHETDSAVATARRPRWLCAGALVLAGGFLLGFLFGWFIKSSNEATNITPKHNMKA 60

Qy     61 FLDELKAENIKKFLYNFTQIPHLAGTEQNFQLAKQIQSQWKEFGLDSVELAHYDVLLSYP 120
Db     61 FLDELKAENIKKFLYNFTQIPHLAGTEQNFQLAKQIQSQWKEFGLDSVELAHYDVLLSYP 120

Qy    121 NKTHPNYISIINEDGNEIFNTSLFEP PPPGYENVSDIVPPFSAFSPQGMPEGDLVYVNYA 180
Db    121 NKTHPNYISIINEDGNEIFNTSLFEP PPPGYENVSDIVPPFSAFSPQGMPEGDLVYVNYA 180

Qy    181 RTEDFFKLERDMKINCSGKIVIRYGVFRGNKVKNQLAGAKGVILYSDPADYFAPGVK 240
Db    181 RTEDFFKLERDMKINCSGKIVIRYGVFRGNKVKNQLAGAKGVILYSDPADYFAPGVK 240

Qy    241 SYPDGWNLPGGGVQQRGNILNLNAGDPLTPGYPANAYARRGIAEAVGLPSIPVHPIGYY 300
Db    241 SYPDGWNLPGGGVQQRGNILNLNAGDPLTPGYPANAYARRGIAEAVGLPSIPVHPIGYY 300

Qy    301 DAQKLEKMGGSAPPDSSWRGSLKVPYNVGPFTGNFSTQKVKMHIHSTNEVTRIYNVIG 360
Db    301 DAQKLEKMGGSAPPDSSWRGSLKVPYNVGPFTGNFSTQKVKMHIHSTNEVTRIYNVIG 360

Qy    361 TLRGAVEPDYVILGGHRDSWVFGGIDPQSGAAVVHEIVRSFGTLKKEGWRPRRTILFAS 420
Db    361 TLRGAVEPDYVILGGHRDSWVFGGIDPQSGAAVVHEIVRSFGTLKKEGWRPRRTILFAS 420

Qy    421 WDAEEFGLLGSTEWAEENSRLQERGVAIYNADSSIEGNYTLRVDCTPLMYSLVHNLTKE 480

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|    |     |                        |                       |            |        |         |              |             |
|----|-----|------------------------|-----------------------|------------|--------|---------|--------------|-------------|
| Db | 421 | WDAEEFGLLGSTEWAEENSRLQ | ERGVAYINADSSIEGNYTLRV | DC         | TP     | LM      | YSLVHNLTKE   | 480         |
| Qy | 481 | LKSPDEGFEGKSLYESWTKKSP | SPEFSGMPRISKLGSGNDFEV | FF         | Q      | RL      | GIASGRARYTKN | 540         |
|    |     |                        |                       |            |        |         |              |             |
| Db | 481 | LKSPDEGFEGKSLYESWTKKSP | SPEFSGMPRISKLGSGNDFEV | FF         | Q      | RL      | GIASGRARYTKN | 540         |
| Qy | 541 | WETNKFSGYPLYHSVYET     | YELVEKFYDPMFKYHLTVAQ  | VR         | GG     | M       | FELANSIVL    | PFDCRDY 600 |
|    |     |                        |                       |            |        |         |              |             |
| Db | 541 | WETNKFSGYPLYHSVYET     | YELVEKFYDPMFKYHLTVAQ  | VR         | GG     | M       | FELANSIVL    | PFDCRDY 600 |
| Qy | 601 | AVVLRKYADKIYISISMKHPQ  | EMKTYSVSFDSLFS        | SAVKNFTEI  | ASKF   | SERLQ   | DFDKSNPIV    | 660         |
|    |     |                        |                       |            |        |         |              |             |
| Db | 601 | AVVLRKYADKIYISISMKHPQ  | EMKTYSVSFDSLFS        | SAVKNFTEI  | ASKF   | SERLQ   | DFDKSNPIV    | 660         |
| Qy | 661 | LRMMNDQLMFLE           | RAFIDPLGLPDRPFYRHVI   | YAPSSHNKY  | AGESFP | PGIYDAL | FDIESKVD     | 720         |
|    |     |                        |                       |            |        |         |              |             |
| Db | 661 | LRMMNDQLMFLE           | RAFIDPLGLPDRPFYRHVI   | YAPSSHNKY  | AGESFP | PGIYDAL | FDIESKVD     | 720         |
| Qy | 721 | PSKAWGEVKRQ            | IYVAAFTVQ             | AAAETLSEVA | 750    |         |              |             |
|    |     |                        |                       |            |        |         |              |             |
| Db | 721 | PSKAWGEVKRQ            | IYVAAFTVQ             | AAAETLSEVA | 750    |         |              |             |